

D-2939CIPCONDIV1

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE  
PATENT

In the application of:	)	
Williams et al	)	Group Art Unit: N/A
	)	(Prior App.: 1648)
	)	
Serial No.	)	Examiner: N/A
N/A	)	(Prior App.: Li, Bao Q.)
Filing Date:	)	
HEREWITH	)	
	)	
For: SOLUBLE RECOMBINANT BOTULINUM	)	
TOXIN PROTEINS	)	

INFORMATION DISCLOSURE STATEMENT

Commissioner for Patents  
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Alexandria, VA 22313

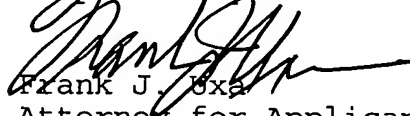
Dear Sir:

Applicant wishes to call to the attention of the Examiner the documents cited on the accompanying Form PTO-1449. No concession is made that these documents are prior art, and applicant expressly reserves the right to antedate the documents as may be appropriate. Applicant requests that each of these documents be made of record in the above-identified application.

All of these documents were cited in related Application Serial No. 08/405,496, filed March 16, 1995 and Application Serial No. 08/704,159, filed August 28, 1996.

Therefore, no copies of these documents are submitted herewith.

Respectfully submitted,

  
Frank J. Uxa  
Attorney for Applicant  
Reg. No. 25,612  
4 Venture, Suite 300  
Irvine, CA 92618  
(949) 450-1750  
Facsimile (949) 450-1764

FJUxa/ac

ORM PTO-1449  
(modified)U.S. Department of Commerce  
Patent and Trademark OfficeAttorney Docket No. D-2434CIPCOSerial No.: n/aINFORMATION DISCLOSURE STATEMENT BY APPLICANT  
(Use Several Sheets If Necessary)Applicant: James A. Williams et al.Filing Date: here with

Group Art Unit:

37 CFR § 1.98(b))

## U.S. PATENT DOCUMENTS

Examiner Initials	Serial / Patent Number	Issue Date	Applicant / Patentee	Class	Subclass	Filing Date
	1	5,080,895	1/14/92	Tokoro		

## OTHER DOCUMENTS (Including Author, Title, Date, Relevant Pages, Place of Publication)

2	Cato et al. (1986) "Clostridium," in <i>Bergey's Manual® of Systematic Bacteriology</i> , 2:1141-1200, Sneath (ed.), Williams & Wilkins
3	Engelkirk et al. (1992) "Classification," in <i>Principles and Practice of Clinical Anaerobic Bacteriology</i> , pp. 22-23, Star Publishing Co., Belmont, CA
4	Stephen and Pietrowski (1986) "Toxins Which Traverse Membranes and Deregulate Cells," in <i>Bacterial Toxins</i> , 2d ed., pp. 66-67, American Society for Microbiology
5	Berkow and Fletcher (eds.) (1992) "Bacterial Diseases," in <i>Merck Manual of Diagnosis and Therapy</i> , 16th ed., pp. 116-126, Merck Research Laboratories, Rahway, NJ.
6	Sigmund and Fraser (eds.) (1979) "Clostridial Infections," in <i>Merck Veterinary Manual</i> , 5th ed., pp. 396-409, Merck & Co., Rahway, NJ.
7	Hatheway (1990) "Bacteriophages and plasmids and their roles in coding for botulinal neurotoxins," <i>Clin. Microbiol. Rev.</i> 3:73-74
8	Arnon (1986) "Infant Botulism: Anticipating the Second Decade," <i>J. Infect. Dis.</i> 154:201-206
9	Arnon (1980) "Infant Botulism," <i>Ann. Rev. Med.</i> 31:541-559
10	MacDonald et al. (1986) "The Changing Epidemiology of Adult Botulism in the United States," <i>Am. J. Epidemiol.</i> 124:794-799
11	Tacket et al. (1984) "Equine Antitoxin Use and Other Factors That Predict Outcome in Type A Foodborne Botulism," <i>Am. J. Med.</i> 76:794-798
12	Swartz (1990) "Anaerobic Spore-Forming Bacilli: The Clostridia," in <i>B.D. Microbiology</i> , 4th edition, pp. 633-646, Davis et al.(eds.), J.B. Lippincott Co.
13	Holzer (1962) "Botulismus durch Inhalation," <i>Med. Klin.</i> 41:1735-738
14	Franz et al. (1993) in <i>Botulinum and Tetanus Neurotoxins</i> , pp. 473-476, B.R. DasGupta, ed., Plenum Press, NY
15	Arnon et al. (1981) "Infant Botulism: Epidemiology and Relation to Sudden Infant Death Syndrome," <i>Epidemiol. Rev.</i> 3:45-66
16	Frankovich and Arnon (1991) "Clinical Trial of Botulism Immune Globulin for Infant Botulism," <i>West. J. Med.</i> 154:103
17	Sugiyama (1980) "Clostridium botulinum Neurotoxin," <i>Microbiol. Rev.</i> 44:419-448
18	Balady (1991) "Botulism Antitoxin Fielded for Operation Desert Storm," <i>USAMRDC Newsletter</i> , p. 6
19	Schwarz and Arnon (1992) "Botulism Immune Globulin for Infant Botulism Arrives-One Year and A Gulf War Later," <i>Western J. Med.</i> 156:197-198
20	Peterson et al. (1979) "The Sudden Infant Death Syndrome and Infant Botulism," <i>Rev. Infect. Dis.</i> 1:630-634
21	Arnon et al. (1978) "Intestinal Infection and Toxin Production by Clostridium Botulinum as One Cause of Sudden Infant Death Syndrome," <i>Lancet</i> , pp. 1273-1277
22	Informational Brochure for the Pentavalent (ABCDE) Botulinum Toxoid, Centers for Disease Control, Rev. 1995, pp. 1-3 and 3 unnumbered pages
23	Brooks et al. (eds.) (1991) "Infections Caused by Anaerobic Bacteria," in <i>Jawetz, Melnick, &amp; Adelberg's Medical Microbiology</i> , 19th ed., pp. 257-262, Appleton & Lange, San Mateo, CA
24	Engelkirk et al. (1992) <i>Principles and Practice of Clinical Anaerobic Bacteriology</i> , pp. 64-67, Star Publishing Co., Belmont, CA
25	Lyerly et al. (1992) "Characterization of a Toxin A-Negative, Toxin B-Positive Strain of Clostridium difficile," <i>Infect. Immun.</i> 60:4633-4639
26	Borriello et al. (1990) "Virulence Factors of Clostridium difficile," <i>Rev. Infect. Dis.</i> , 12(Suppl. 2):S185-S191
27	Lyerly et al. (1985) "Effects of Clostridium difficile Toxins Given Intragastrically to Animals," <i>Infect. Immun.</i> 47:349-352

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Initial citation considered. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

FORM PTO-1449  
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## OTHER DOCUMENTS (Including Author, Title, Date, Relevant Pages, Place of Publication)

- |    |   |
|----|---|
| 28 | Rolfe (1990) "Binding Kinetics of <i>Clostridium difficile</i> Toxins A and B to Intestinal Brush Border Membrane: from Infant and Adult Hamsters," <i>Infect. Immun.</i> 59:1223-1230  |
| 29 | Kim and Rolfe (1987) "The Protective Role of Antibody to Toxin A in <i>Clostridium difficile</i> - Induced Ileocectitis," <i>Abstr. Ann. Meet. Am. Soc. Microbiol.</i> 69:62  |
| 30 | Banno <i>et al.</i> (1984) "Biochemical Characterization and Biologic Actions of Two Toxins (D-1 and D-2) From <i>Clostridium difficile</i> ," <i>Rev. Infect. Dis.</i> 6(Suppl. 1:S11-S20)   |
| 31 | Rihn <i>et al.</i> (1984) "A New Purification Procedure for <i>Clostridium difficile</i> Enterotoxin," <i>Biochem. Biophys. Res. Comm.</i> 124:690-695  |
| 32 | Justus <i>et al.</i> (1982) "Myoelectric Effects of <i>Clostridium difficile</i> : Motility-Altering Factors Distinct From its Cytotoxin and Enterotoxin in Rabbits," <i>Gastroenterol.</i> 83:836-843  |
| 33 | Finegold <i>et al.</i> (1992) "Antimicrobial-Associated Pseudomembranous Colitis," in <i>Clinical Guide to Anaerobic Infections</i> , pp. 88-89, Star Publishing Co., Belmont, CA   |
| 34 | United States Pharmacopeia (1990) United States Pharmacopeial Convention, Vol. XXII:1515-1516 Rockville, MD   |
| 35 | FDA Guidelines for Parenteral Drugs (December 1987) <i>i.e.</i> , <i>Guideline on Validation of the Limulus Amebocyte Lysate Test as an End-Product Endotoxin Test for Human and Animal Parenteral Drugs, Biological Products and Medical Devices</i> |
| 36 | Pearson (1985) "Equivalency of LAL and USP Rabbit Pyrogen Tests," in <i>Pyrogens: endotoxins, lal testing and depyrogenation</i> , Marcel Dekker, NY, pp. 150-155   |
| 37 | Minton (1995) "Molecular Genetics of Clostridial Neurotoxins," <i>Curr. Top. Microbiol. Immunol.</i> 195:161-194  |
| 38 | Benedict and Yamaga (1966) "Immunoglobulins and Antibody Production in Avian Species," in <i>Comparative Immunology</i> , pp. 335-375 (J.J. Marchaloni, ed.), Blackwell, Oxford   |
| 39 | Patterson <i>et al.</i> (1962) "Antibody Production and Transfer to Egg Yolk in Chickens," <i>Immunol.</i> 89:272-278   |
| 40 | Carroll and Stollar (1983) "Antibodies of Calf Thymus RNA Polymerase II from Egg Yolks of Immunized Hens," <i>J. Biol. Chem.</i> 258:24-26  |
| 41 | Polsón <i>et al.</i> (1980) "Antibodies to Proteins from Yolk of Immunized Hens," <i>Immunol. Comm.</i> 9:495-514   |
| 42 | DasGupta and Sugiyama (1972) "A Common Subunit Structure In <i>Clostridium Botulinum</i> Type A, B, and E Toxins," <i>Biochem. Biophys. Res. Commun.</i> 48:108-112   |
| 43 | DasGupta (1990) "Structure and Biological Activity of Botulinum Neurotoxin," <i>J. Physiol.</i> 84:220-228  |
| 44 | Halpern and Loftus (1993) "Characterization of the Receptor-binding Domain of Tetanus Toxin," <i>J. Biol. Chem.</i> 268:11188-11192   |
| 45 | Whelan <i>et al.</i> (1992) "Molecular Cloning of the <i>Clostridium botulinum</i> Structural Gene Encoding the Type B Neurotoxin and Determination of Its Entire Nucleotide Sequence," <i>Appl. Environ. Microbiol.</i> 58:2345-2354                 |
| 46 | Sakaguchi (1983) " <i>Clostridium Botulinum</i> Toxins," <i>Pharmac. Ther.</i> 19:165-194   |
| 47 | Moberg and H. Sugiyama (1978) "Affinity Chromatography Purification of Type A Botulinum Neurotoxin from Crystalline Toxic Complex," <i>Appl. Environ. Microbiol.</i> 35:878-880   |
| 48 | Thalley <i>et al.</i> (1993) "Development of an Avian Antitoxin to Type A Botulinum Neurotoxin," in <i>Botulinum and Tetanus Neurotoxins</i> , pp. 467-472, B.R. DasGupta, ed., Plenum Press, NY  |
| 49 | Schantz and Johnson (1992) "Properties and Use of Botulinum Toxin and Other Microbial Neurotoxins in Medicine," <i>Microbiol. Rev.</i> 56:80-99   |
| 50 | Makoff <i>et al.</i> (1989) "Expression of Tetanus Toxin Fragment C in <i>E. Coli</i> : Its Purification and Potential Use as a Vaccine," <i>Bio/Technology</i> 7:1043-1046   |
| 51 | Makoff <i>et al.</i> (1989) "Expression of tetanus toxin fragment C in <i>E. coli</i> : high level expression by removing rare codons," <i>Nucl. Acids Res.</i> 17:10191-10202  |

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## OTHER DOCUMENTS (Including Author, Title, Date, Relevant Pages, Place of Publication)

52	Halpern <i>et al.</i> (1990) "Cloning and Expression of Functional Fragment C of Tetanus Toxin," <i>Infect. Immun.</i> 58:1004-1009
53	Romanos <i>et al.</i> (1991) "Expression of tetanus toxin fragment C in yeast: gene synthesis is required to eliminate fortuitous polyadenylation sites in AT-rich DNA," <i>Nucleic Acids Res.</i> 19:1461-1467
54	Charles <i>et al.</i> (1991) "Synthesis of Tetanus Toxin Fragment C in Insect Cells by Use of a Baculovirus Expression System," <i>Infect. Immun.</i> 59:1627-1632
55	Popoff <i>et al.</i> (1991) "Characterization of the C3 Gene of <i>Clostridium botulinum</i> Types C and D and Its Expression in <i>Escherichia coli</i> ," <i>Infect. Immun.</i> 59:3673-3679
56	LaPenotiere <i>et al.</i> (1993) "Development of a Molecular Engineered Vaccine for <i>C. Botulinum</i> Neurotoxins," in <i>Botulinum and Tetanus Neurotoxins</i> , B.R. DasGupta, ed., Plenum Press, NY, pp. 463-466
57	Thompson <i>et al.</i> (1990) "The complete amino acid sequence of the <i>Clostridium botulinum</i> type A neurotoxin, deduced by nucleotide sequence analysis of the encoding gene," <i>Eur. J. Biochem.</i> 189:73-81
58	LaPenotiere <i>et al.</i> (1995) "Expression of a Large, Nontoxic Fragment of Botulinum Neurotoxin Serotype A and Its Use as an Immunogen," <i>Toxicon</i> . 33:1383-1386
59	Middlebrook and Brown (1995) "Immunodiagnosis and Immunotherapy of Tetanus and Botulinum Neurotoxins," <i>Curr. Top. Microbiol. Immunol.</i> 195:89-122
60	Hutson <i>et al.</i> (1994) "Nucleotide Sequence of the Gene Coding for Non-Proteolytic <i>Clostridium botulinum</i> Type B Neurotoxin: Comparison with Other Clostridial Neurotoxins," <i>Curr. Microbiol.</i> 28:101-110
61	Poulet <i>et al.</i> (1992) "Sequences of the Botulin Neurotoxin E Derived from <i>Clostridium Botulinum</i> Type E (Strain Beluga) and <i>Clostridium Butyricum</i> (Strains ATCC 43181 and ATCC 43755)," <i>Biochem. Biophys. Res. Commun.</i> 183:107-113
62	Whelan <i>et al.</i> (1992) "The complete amino acid sequence of the <i>Clostridium botulinum</i> type-E neurotoxin, derived by nucleotide-sequence analysis of the encoding gene," <i>Eur. J. Biochem.</i> 204:657-667
63	Fujii <i>et al.</i> (1993) "The complete nucleotide sequence of the gene encoding the nontoxic component of <i>Clostridium botulinum</i> type E progenitor toxin," <i>J. Gen. Microbiol.</i> 139:79-86
64	Delmee <i>et al.</i> (1990) "Characterization of Flagells of <i>Clostridium difficile</i> and Their Role in Serogrouping Reactions," <i>J. Clin. Microbiol.</i> 28:2210-2214
65	Delmee and Avesani (1990) "Virulence of ten serogroups of <i>Clostridium difficile</i> in hamsters," <i>J. Med Microbiol.</i> 33:85-90
66	Toma <i>et al.</i> (1988) "Serotyping of <i>Clostridium difficile</i> ," <i>J. Clin. Microbiol.</i> 26:426-428
67	Delmee <i>et al.</i> (1985) "Serogrouping of <i>Clostridium difficile</i> Strains by Slide Agglutination," <i>J. Clin. Microbiol.</i> 21:323-327
68	Davies and Borriello (1990) "Detection of Capsule in Strains of <i>Clostridium difficile</i> of Varying Virulence and Toxigenicity," <i>Microbial Path.</i> 9:141-146
69	Edelstein (1990) "Processing Clinical Specimens for Anaerobic Bacteria: Isolation and Identification Procedures," in <i>Bailey and Scott's Diagnostic Microbiology</i> , pp. 477-507, C.V. Mosby Co. Baron and Finegold (eds.)
70	Padhye <i>et al.</i> (1990) "Production and Characterization of a Monoclonal Antibody Specific for Enterohemorrhagic <i>Escherichia coli</i> of Serotypes O157:H7 and O26:H11," <i>J. Clin. Microbiol.</i> 29:99-103
71	Lyerly <i>et al.</i> (1991) "Passive Immunization of Hamsters Against Disease Caused by <i>Clostridium difficile</i> by Use of Bovine Immunoglobulin G Concentrate," <i>Infect. Immun.</i> 59:2215-2218
72	DasGupta & Sathymoorthy (1984) "Purification and Amino Acid Composition of Type A Botulinum Neurotoxin," <i>Toxicon</i> , 22:415-424
73	Singh & DasGupta (1989) "Molecular Differences Between Type A Botulinum Neurotoxin and Its Toxoid," <i>Toxicon</i> 27:403-410

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## OTHER DOCUMENTS (Including Author, Title, Date, Relevant Pages, Place of Publication)

74	Towbin <i>et al.</i> (1979) "Electrophoretic Transfer of Proteins from Polyacrylamide Gels to Nitrocellulose Sheets: Procedure and Some Applications," <i>Proc. Natl. Acad. Sci. USA</i> , 76:4350-4354
75	Weber and Osborn (1975) "Proteins and Sodium Dodecyl Sulfate: Molecular Weight Determination on Polyacrylamide Gels and Related Procedures," in <i>The Proteins</i> , pp. 179-223, 3d Edition (H. Neurath & R.L. Hill, eds), Academic Press, NY
76	Carroll and Laughon (1987) "Production and purification of polyclonal antibodies to the foreign segment of $\beta$ -galactosidase fusion proteins," in <i>DNA Cloning: A Practical Approach</i> , Vol.III, pp. 89-111, D. Glover (ed.) IRL Press, Oxford
77	Thalley and Carroll (1990) "Rattlesnake and Scorpion Antivenoms From The Egg Yolks of Immunized Hens," <i>Bio/Technology</i> 8:934-938
78	Ohishi <i>et al.</i> (1977) "Oral Toxicities of <i>Clostridium botulinum</i> Toxins in Response to Molecular Size," <i>Infect. Immun.</i> 16:106-107
79	Wren <i>et al.</i> (1991) "Antigenic Cross-Reactivity and Functional Inhibition by Antibodies to <i>Clostridium difficile</i> Toxin A, <i>Streptococcus mutans</i> Glucan-Binding Protein, and a Synthetic Peptide," <i>Infect. Immun.</i> 59:3151-3155
80	Ehrich <i>et al.</i> (1980) "Production of <i>Clostridium difficile</i> Antitoxin," <i>Infect. Immun.</i> 28:1041-1043
81	McGee <i>et al.</i> (1992) "Local induction of tumor necrosis factor as a molecular mechanism of mucosal damage by gonococci," <i>Microb. Path.</i> 12:333-341
82	Fekety (1986) "Animal Models of Antibiotic-Induced Colitis," in <i>Experimental Models in Antimicrobial Chemotherapy</i> , 2:61-72, Zak and Sande (eds.), Harcourt Brace Jovanovich, NY
83	Borriello <i>et al.</i> (1987) " <i>Clostridium difficile</i> -a spectrum of virulence and analysis of putative virulence determinants in the hamster model of antibiotic-associated colitis," <i>J. Med. Microbiol.</i> 24:53-64
84	Kim <i>et al.</i> (1987) "Immunization of Adult Hamsters Against <i>Clostridium difficile</i> -Associated Ileoceitis and Transfer of Protection to Infant Hamsters," <i>Infect. Immun.</i> 55:2984-2992
85	Borriello <i>et al.</i> (1988) " <i>Mucosal Association by Clostridium difficile</i> in the hamster gastrointestinal tract," <i>J. Med. Microbiol.</i> 25:191-196
86	Dove <i>et al.</i> (1990) "Molecular Characterization of the <i>Clostridium difficile</i> Toxin A Gene," <i>Infect. Immun.</i> 58:480-488
87	Williams <i>et al.</i> (1995) "Expression of foreign proteins in <i>E. coli</i> using plasmid vectors and purification of specific polyclonal antibodies," in <i>DNA Cloning 2: Expression Systems</i> , pp. 15-58, Glover and Hames (eds.) IRL Press, Oxford
88	von Eichel-Streiber and Sauerborn (1990) " <i>Clostridium difficile</i> Toxin A Carries a C-Terminal Repetitive Structure Homologous to the Carbohydrate Binding Region of Streptococcal Glycosyltransferases," <i>Gene</i> 96:107-113
89	Wren and Tabaqchali (1987) "Restriction Endonuclease DNA Analysis of <i>Clostridium difficile</i> ," <i>J. Clin. Microbiol.</i> 25:2402-2404
90	Price <i>et al.</i> (1987) "Cloning of the Carbohydrate-binding Portion of the Toxin A Gene of <i>Clostridium difficile</i> ," <i>Curr. Microbiol.</i> 16:55-60
91	Krivan <i>et al.</i> (1986) "Cell Surface Binding Site for <i>Clostridium difficile</i> Enterotoxin: Evidence for a Glycoconjugate Containing the Sequence Gal $\alpha$ 1-3Gal $\beta$ 1-4GlcNAc," <i>Infect. Immun.</i> , 53:573-581
92	von Eichel-Streiber <i>et al.</i> (1989) "Cloning and Characterization of Overlapping DNA Fragments of the Toxin A Gene of <i>Clostridium difficile</i> ," <i>J. Gen. Microbiol.</i> 135:55-64
93	Lyerly <i>et al.</i> (1989) "Nonspecific Binding of Mouse Monoclonal Antibodies to <i>Clostridium difficile</i> Toxins A and B," <i>Curr. Microbiol.</i> 19:303-306
94	Lyerly <i>et al.</i> (1990) "Vaccination Against Lethal <i>Clostridium difficile</i> Enterocolitis with a Nontoxic Recombinant Peptide of Toxin A," <i>Curr. Microbiol.</i> 21:29-32
95	Swanson <i>et al.</i> (1991) "In Vitro and In Vivo Evaluation of Tiamcins B and C Against <i>Clostridium difficile</i> ," <i>Antimicro. Agents and Chemo.</i> 35:1108-1111
96	Swanson <i>et al.</i> (1989) "Phenelfamycins, a Novel Complex of Efamycin-type Antibiotics, III. Activity In Vitro and in a Hamster Colitis Model," <i>J. Antibiotics</i> 42:94-101

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|-----|---|
| 97  | von Eichel-Streiber <i>et al.</i> (1992) "Comparative Sequence Analysis of the <i>Clostridium difficile</i> Toxins A and B," Molec. Gen. Genetics 233:260-268   |
| 98  | Barroso <i>et al.</i> (1990) "Nucleotide Sequence of <i>Clostridium difficile</i> Toxin B Gene," Nucl. Acids Res. 18:4004   |
| 99  | Thompson <i>et al.</i> (1990) "The complete amino acid sequence of the <i>Clostridium botulinum</i> type A neurotoxin, deduced by nucleotide sequence analysis of the encoding gene," Eur. J. Biochem. 189:73-81  |
| 100 | Riggs (1989) in <i>Current Protocols in Molecular Biology</i> , Vol. 2, Ausubel, <i>et al.</i> (Eds.) pp. 16.6.1-16.6.14  |
| 101 | Schantz and Kautter (1978) "Microbiological Methods: Standardized Assay for <i>Clostridium botulinum</i> Toxins," J. AOAC 61:96-99  |
| 102 | Investigational New Drug (BB-IND-3703) application by the Surgeon General of the Department of the Army to the Federal Food and Drug Administration   |
| 103 | Pearson (1985) <i>Pyrogens: endotoxins, LAL testing and depyrogenation</i> , Marcel Dekker, NY, pp. 23-56   |
| 104 | Smith and Corcoran (1994) "Expression and Purification of Glutathione-S-Transferase Fusion Proteins," Current Protocols in Molecular Biology, Supplement 28:16.7.1-16.7.7   |
| 105 | Gragerov <i>et al.</i> (1992) "Cooperation of GroEL/GroES and DnaK/DnaJ heat shock proteins in preventing protein misfolding in <i>Escherichia coli</i> ," Proc. Natl. Acad. Sci. USA 89:10341-10344  |
| 106 | Fujii <i>et al.</i> (1990) "The Nucleotide and Deduced Amino Acid Sequences of <i>EcoRI</i> Fragment Containing the 5'-Terminal Region of <i>Clostridium botulinum</i> Type E Toxin Gene Cloned from Mashike, Iwanai and Otaru Strains," Microbiol. Immunol. 34:1041-1047 |
| 107 | Kimura <i>et al.</i> (1990) "The Complete Nucleotide Sequence of the Gene Coding for Botulinum Type C <sub>1</sub> Toxin in the C-St Phage Genome," Biochem. Biophys. Res. Comm. 171:1304-1311  |
| 108 | Sunagawa <i>et al.</i> (1992) "The Complete Amino Acid Sequence of the <i>Clostridium botulinum</i> Type D Neurotoxin, Deduced by Nucleotide Sequence Analysis of the Encoding Phage d-16 $\phi$ Genome," J. Vet. Med. Sci. 54:905-913                                    |
| 109 | Binz <i>et al.</i> (1990) "Nucleotide sequence of the gene encoding <i>Clostridium botulinum</i> neurotoxin type D," Nucleic Acids Res. 18:5556   |
| 110 | Campbell <i>et al.</i> (1993) "Nucleotide sequence of the gene coding for <i>Clostridium botulinum</i> ( <i>Clostridium argentinense</i> ) type G neurotoxin: genealogical comparison with other clostridial neurotoxins," Biochim. Biophys. Acta 1216:487-491            |
| 111 | East <i>et al.</i> (1992) "Sequence of the gene encoding type F neurotoxin of <i>Clostridium botulinum</i> ," FEMS Micro. Letters 96:225-230  |
| 112 | Niemann (1992) "Clostridial Neurotoxins - Proposal of a Common Nomenclature," Toxicon 30:223-225  |
| 113 | Food and Drug Administration Document (Docket No. 79D-0465) 53 FR 5044, February 19, 1988   |
| 114 | Food and Drug Administration Document (Docket No. 79D-0465) 48 FR 27835, June 17, 1983  |

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**FOREIGN PATENT DOCUMENTS**

	DOCUMENT NUMBER							DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION	
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**OTHER DOCUMENTS**

		Plotkin et al., Vaccines, published by W.B. Saunders Company, Philadelphia, p. 571 (1988)
		Nygren, P.-A. Et al. Trends in Biotechnology 12(5): 184-188

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